LODOSYN - carbidopa tablet
Bristol-Myers Squibb Company

When LODOSYN* (Carbidopa) is to be given to carbidopa-naive patients who are being treated with levodopa, the two drugs should be given at the same time, starting with no more than 20 to 25% of the previous daily dosage of levodopa when given without LODOSYN (Carbidopa). At least twelve hours should elapse between the last dose of levodopa and initiation of therapy with LODOSYN (Carbidopa) and levodopa. See the WARNINGS and DOSAGE AND ADMINISTRATION sections before initiating therapy.

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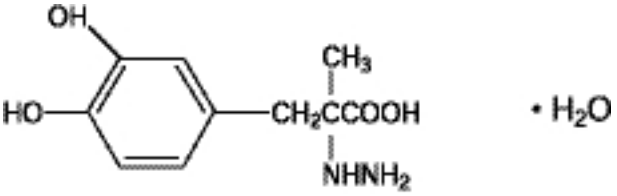
DESCRIPTION

Carbidopa, an inhibitor of aromatic amino acid decarboxylation, is a white, crystalline compound, slightly soluble in water, with a molecular weight of 244.3. It is designated chemically as (–)-L-α-hydrazino-α-methyl-β-(3,4-dihydroxybenzene) propanoic acid monohydrate. Its empirical formula is $C_{10}H_{14}N_2O_4 \cdot H_2O$, and its structural formula is:



LODOSYN (Carbidopa) tablets contain 25 mg of carbidopa. Inactive ingredients are cellulose, FD&C Yellow 6, magnesium stearate and starch.
Tablet content is expressed in terms of anhydrous carbidopa which has a molecular weight of 226.3.

CLINICAL PHARMACOLOGY

Parkinson's disease is a progressive, neurodegenerative disorder of the extrapyramidal nervous system affecting the mobility and control of the skeletal muscular system. Its characteristic features include resting tremor, rigidity, and bradykinetic movements. Symptomatic treatments, such as levodopa therapies, may permit the patient better mobility.

Mechanism of Action

Current evidence indicates that symptoms of Parkinson's disease are related to depletion of dopamine in the corpus striatum. Administration of dopamine is ineffective in the treatment of Parkinson's disease apparently because it does not cross the blood-brain barrier. However, levodopa, the metabolic precursor of dopamine, does cross the blood-brain barrier, and presumably is converted to dopamine in the brain. This is thought to be the mechanism whereby levodopa relieves symptoms of Parkinson's disease.

Pharmacodynamics

When levodopa is administered orally it is rapidly decarboxylated to dopamine in extracerebral tissues so that only a small portion of a given dose is transported unchanged to the central nervous system. For this reason, large doses of levodopa are required for adequate therapeutic effect and these may often be accompanied by nausea and other adverse reactions, some of which are attributable to dopamine formed in extracerebral tissues.
The incidence of levodopa-induced nausea and vomiting is less when LODOSYN is used with levodopa than when levodopa is used without LODOSYN. In many patients this reduction in nausea and vomiting will permit more rapid dosage titration.
Carbidopa inhibits decarboxylation of peripheral levodopa. Carbidopa has not been demonstrated to have any overt pharmacodynamic actions in the recommended doses. It does not appear to cross the blood-brain barrier readily and does not affect the metabolism of levodopa within the central nervous system at doses of carbidopa that are recommended for maximum effective inhibition of peripheral decarboxylation of levodopa.
Since its decarboxylase-inhibiting activity is limited primarily to extracerebral tissues, administration of carbidopa with levodopa makes more levodopa available for transport to the brain. However, since levodopa and carbidopa compete with certain amino acids for transport across the gut wall, the absorption of levodopa and carbidopa may be impaired in some patients on a high protein diet.

Pharmacokinetics

Carbidopa reduces the amount of levodopa required to produce a given response by about 75% and, when administered with levodopa, increases both plasma levels and the plasma half-life of levodopa, and decreases plasma and urinary dopamine and homovanillic acid. In clinical pharmacologic studies, simultaneous administration of separate tablets of carbidopa and levodopa produced greater urinary excretion of levodopa in proportion to the excretion of dopamine when compared to the two drugs administered at separate times.

Supplemental pyridoxine (vitamin B_6) can be given to patients when they are receiving carbidopa and levodopa concomitantly or as SINEMET* CR (Carbidopa-Levodopa) Sustained-Release or SINEMET* (Carbidopa-Levodopa). Previous reports in the medical literature cautioned that high doses of vitamin B_6 should not be taken by patients on levodopa therapy alone because exogenously administered pyridoxine would enhance the metabolism of levodopa to dopamine. The introduction of carbidopa to levodopa therapy, which inhibits the peripheral decarboxylation of levodopa to dopamine, counteracts the metabolic-enhancing effect of pyridoxine. Carbidopa is combined with levodopa in SINEMET (Carbidopa-Levodopa) and SINEMET CR (Carbidopa-Levodopa) Sustained-Release tablets. These combination tablets are available in three strengths for SINEMET: SINEMET 10-100 (Carbidopa-Levodopa), SINEMET 25-250 (Carbidopa-Levodopa) (1:10 ratio of carbidopa to levodopa) and SINEMET 25-100 (Carbidopa-Levodopa) (1:4 ratio of carbidopa to levodopa), and in two strengths for SINEMET CR: SINEMET CR 50-200 (Carbidopa-Levodopa) Sustained-Release and SINEMET CR 25-100 (Carbidopa-Levodopa) Sustained-Release (1:4 ratio of carbidopa to levodopa). Clinical trials show that these ratios of carbidopa and levodopa provide useful therapeutic effects in most patients.

INDICATIONS AND USAGE

LODOSYN is indicated for use with SINEMET (Carbidopa-Levodopa) or with levodopa in the treatment of the symptoms of idiopathic Parkinson's disease (paralysis agitans), postencephalitic parkinsonism, and symptomatic parkinsonism which may follow injury to the nervous system by carbon monoxide intoxication and/or manganese intoxication.

LODOSYN is for use with SINEMET (Carbidopa-Levodopa) in patients for whom the dosage of SINEMET (Carbidopa-Levodopa) provides less than adequate daily dosage (usually 70 mg daily) of carbidopa.

LODOSYN is for use with levodopa in the occasional patient whose dosage requirement of carbidopa and levodopa necessitates separate titration of each entity.

LODOSYN is used with SINEMET (Carbidopa-Levodopa) or with levodopa to permit the administration of lower doses of levodopa with reduced nausea and vomiting, more rapid dosage titration, and with a somewhat smoother response. However, patients with markedly irregular ("on-off") responses to levodopa have not been shown to benefit from the addition of carbidopa.

Since carbidopa prevents the reversal of levodopa effects caused by pyridoxine, supplemental pyridoxine (vitamin B_6), can be given to patients when they are receiving carbidopa and levodopa concomitantly or as SINEMET (Carbidopa-Levodopa).

Although the administration of LODOSYN permits control of parkinsonism and Parkinson's disease with much lower doses of levodopa, there is no conclusive evidence at present that this is beneficial other than in reducing nausea and vomiting, permitting more rapid titration, and providing a somewhat smoother response to levodopa.

Certain patients who responded poorly to levodopa alone have improved when carbidopa and levodopa were given concurrently. This was most likely due to decreased peripheral decarboxylation of levodopa rather than to a primary effect of carbidopa on the peripheral nervous system. Carbidopa has not been shown to enhance the intrinsic efficacy of levodopa.

In considering whether to give LODOSYN with SINEMET (Carbidopa-Levodopa) or with levodopa to patients who have nausea and/or vomiting, the physician should be aware that, while many patients may be expected to improve, some may not. Since one cannot predict which patients are likely to improve, this can only be determined by a trial of therapy. It should be further noted that in controlled trials comparing carbidopa and levodopa with levodopa alone, about half the patients with nausea and/or vomiting on levodopa alone improved spontaneously despite being retained on the same dose of levodopa during the controlled portion of the trial.

CONTRAINDICATIONS

LODOSYN is contraindicated in patients with known hypersensitivity to any component of this drug.

Nonselective monoamine oxidase (MAO) inhibitors are contraindicated for use with levodopa or carbidopa-levodopa combination products with or without LODOSYN. These inhibitors must be discontinued at least two weeks prior to initiating therapy with levodopa. SINEMET (Carbidopa-Levodopa), or levodopa may be administered concomitantly with the manufacturer's recommended dose of an MAO inhibitor with selectivity for MAO type B (e.g., selegiline HCl) (see **PRECAUTIONS, Drug Interactions**).

Levodopa or carbidopa-levodopa products, with or without LODOSYN, are contraindicated in patients with narrow-angle glaucoma.

Because levodopa or carbidopa-levodopa products, with or without LODOSYN, may activate a malignant melanoma, they should not be used in patients with suspicious, undiagnosed skin lesions or a history of melanoma.

WARNINGS

LODOSYN (Carbidopa) has no antiparkinsonian effect when given alone. It is indicated for use with SINEMET (Carbidopa-Levodopa) or levodopa. LODOSYN (Carbidopa) does not decrease adverse reactions due to central effects of levodopa. When LODOSYN (Carbidopa) is to be given to carbidopa-naive patients who are being treated with levodopa alone, the two drugs should be given at the same time. At least twelve hours should elapse between the last dose of levodopa and initiation of therapy with LODOSYN (Carbidopa) and levodopa in combination. Start with no more than one-fifth (20%) to one-fourth (25%) of the previous daily dosage of levodopa when given without LODOSYN (Carbidopa). See the DOSAGE AND ADMINISTRATION section before initiating therapy.

As with levodopa, concomitant administration of LODOSYN and levodopa may cause involuntary movements and mental disturbances. These reactions are thought to be due to increased brain dopamine following administration of levodopa. All patients should be observed carefully for the development of depression with concomitant suicidal tendencies. Patients with past or current

psychoses should be treated with caution. *Because* LODOSYN (Carbidopa) *permits more levodopa to reach the brain and, thus, more dopamine to be formed, dyskinesias may occur at lower levodopa dosages and sooner with concomitant use of* LODOSYN (Carbidopa) *and levodopa or carbidopa-levodopa combination products than with levodopa alone.* The occurrence of dyskinesias may require levodopa dosage reduction.

Levodopa, with or without LODOSYN, should be administered cautiously to patients with severe cardiovascular or pulmonary disease, bronchial asthma, renal, hepatic, or endocrine disease.

Care should be exercised in administering levodopa, with or without LODOSYN, to patients with a history of myocardial infarction who have residual atrial, nodal, or ventricular arrhythmias. In such patients, cardiac function should be monitored with particular care during the period of initial dosage adjustment, in a facility with provisions for intensive cardiac care.

As with levodopa alone there is a possibility of upper gastrointestinal hemorrhage in patients with a history of peptic ulcer.

Neuroleptic Malignant Syndrome (NMS): Sporadic cases of a symptom complex resembling NMS have been reported in association with dose reductions or withdrawal of certain antiparkinsonian agents such as levodopa, SINEMET (Carbidopa-Levodopa), or SINEMET CR (Carbidopa-Levodopa) Sustained-Release. Therefore, patients should be observed carefully when the dosage of levodopa is reduced abruptly or discontinued, especially if the patient is receiving neuroleptics.
NMS is an uncommon but life-threatening syndrome characterized by fever or hyperthermia. Neurological findings, including muscle rigidity, involuntary movements, altered consciousness, mental status changes; other disturbances, such as autonomic dysfunction, tachycardia, tachypnea, sweating, hyper- or hypotension; laboratory findings, such as creatine phosphokinase elevation, leukocytosis, myoglobinuria, and increased serum myoglobin, have been reported.
The early diagnosis of this condition is important for the appropriate management of these patients. Considering NMS as a possible diagnosis and ruling out other acute illnesses (e.g., pneumonia, systemic infection, etc.) is essential. This may be especially complex if the clinical presentation includes both serious medical illness and untreated or inadequately treated extrapyramidal signs and symptoms (EPS). Other important considerations in the differential diagnosis include central anticholinergic toxicity, heat stroke, drug fever, and primary central nervous system (CNS) pathology.
The management of NMS should include: 1) intensive symptomatic treatment and medical monitoring and 2) treatment of any concomitant serious medical problems for which specific treatments are available. Dopamine agonists, such as bromocriptine, and muscle relaxants, such as dantrolene, are often used in the treatment of NMS; however, their effectiveness has not been demonstrated in controlled studies.

PRECAUTIONS

General
As with levodopa alone, periodic evaluations of hepatic, hematopoietic, cardiovascular, and renal function are recommended during extended concomitant therapy with LODOSYN and levodopa, or with LODOSYN and SINEMET (Carbidopa-Levodopa), or any combination of these drugs.
Patients with chronic wide-angle glaucoma may be treated cautiously with LODOSYN and levodopa or SINEMET, or any combination of these drugs, just as with levodopa alone, provided the intraocular pressure is well controlled and the patient is monitored carefully for changes in intraocular pressure during therapy.

Laboratory Tests
Abnormalities in laboratory tests may include elevations of liver function tests such as alkaline phosphatase, SGOT (AST), SGPT (ALT), lactic dehydrogenase, and bilirubin. Abnormalities in blood urea nitrogen and positive Coombs test have also been reported. Commonly, levels of blood urea nitrogen, creatinine, and uric acid are lower during concomitant administration of carbidopa and levodopa than with levodopa alone.
Levodopa and carbidopa-levodopa combination products may cause a false-positive reaction for urinary ketone bodies when a test tape is used for determination of ketonuria. This reaction will not be altered by boiling the urine specimen. False-negative tests may result with the use of glucose-oxidase methods of testing for glucosuria.

Drug Interactions
Caution should be exercised when the following drugs are administered concomitantly with LODOSYN (Carbidopa) *given with levodopa or carbidopa-levodopa combination products.*
Symptomatic postural hypotension has occurred when LODOSYN, given with levodopa or carbidopa-levodopa combination products, was added to the treatment of a patient receiving antihypertensive drugs. Therefore, when therapy with LODOSYN, given with or without levodopa or carbidopa-levodopa combination products, is started, dosage adjustment of the antihypertensive drug may be required.
For patients receiving monoamine oxidase inhibitors, see **CONTRAINDICATIONS**. Concomitant therapy with selegiline and carbidopa-levodopa may be associated with severe orthostatic hypotension not attributable to carbidopa-levodopa alone (see **CONTRAINDICATIONS**).

There have been rare reports of adverse reactions, including hypertension and dyskinesia, resulting from the concomitant use of tricyclic antidepressants and carbidopa-levodopa preparations.
Dopamine D_2 receptor antagonists (e.g., phenothiazines, butyrophenones, risperidone) and isoniazid may reduce the therapeutic effects of levodopa. In addition, the beneficial effects of levodopa in Parkinson's disease have been reported to be reversed by phenytoin and papaverine. Patients taking these drugs with LODOSYN and levodopa or carbidopa-levodopa combination products should be carefully observed for loss of therapeutic response.
Iron salts may reduce the bioavailability of carbidopa and levodopa. The clinical relevance is unclear.
Although metoclopramide may increase the bioavailability of levodopa by increasing gastric emptying, metoclopramide may also adversely affect disease control by its dopamine receptor antagonistic properties.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis
There were no significant differences between treated and control rats with respect to mortality or neoplasia in a 96-week study of carbidopa at oral doses of 25, 45, or 135 mg/kg/day.

Combinations of carbidopa and levodopa (10-20, 10-50, 10-100 mg/kg/day) were given orally to rats for 106 weeks. No effect on mortality or incidence and type of neoplasia was seen when compared to concurrent controls.

Mutagenesis
Mutagenicity studies have not been performed with either carbidopa or the combination of carbidopa and levodopa.

Fertility
Carbidopa had no effect on the mating performance, fertility, or survival of the young when administered orally to rats at doses of 30, 60, or 120 mg/kg/day. The highest dose caused a moderate decrease in body weight gain in males.

The administration of carbidopa-levodopa at dose levels of 10-20, 10-50, or 10-100 mg/kg/day did not adversely affect the fertility of male or female rats, their reproductive performance, or the growth and survival of the young.

Pregnancy

Pregnancy Category C
There are no adequate and well-controlled studies with LODOSYN in pregnant women. It has been reported from individual cases that levodopa crosses the human placental barrier, enters the fetus, and is metabolized. Carbidopa concentrations in fetal tissue appeared to be minimal. LODOSYN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Carbidopa, at doses as high as 120 mg/kg/day, was without teratogenic effects in the mouse or rabbit. In the rabbit, but not in the mouse, carbidopa-levodopa produced visceral anomalies, similar to those seen with levodopa alone, at approximately 7 times the maximum recommended human dose. The teratogenic effect of levodopa in rabbits was unchanged by the concomitant administration of carbidopa.

Nursing Mothers
It is not known whether carbidopa is excreted in human milk. Because many drugs are excreted in human milk, and because of their potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the nursing woman.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established, and use of the drug in patients below the age of 18 is not recommended.

ADVERSE REACTIONS
Carbidopa has not been demonstrated to have any overt pharmacodynamic actions in the recommended doses. The only adverse reactions that have been observed have been with concomitant use of carbidopa with other drugs such as levodopa, and with carbidopa-levodopa combination products.
When LODOSYN is administered concomitantly with levodopa or carbidopa-levodopa combination products, the most common adverse reactions have included dyskinesias such as choreiform, dystonic, and other involuntary movements, and nausea. Other adverse reactions reported with LODOSYN when administered concomitantly with levodopa alone or carbidopa-levodopa combination products were psychotic episodes including delusions, hallucinations, and paranoid ideation, depression with or without development of suicidal tendencies, and dementia. Convulsions also have occurred; however, a causal relationship with concomitant use of LODOSYN and levodopa has not been established.

The following other adverse reactions have been reported with levodopa and carbidopa-levodopa combination products. These same adverse reactions may also occur when LODOSYN is administered with these products.
Body as a Whole: abdominal pain and distress, asthenia, chest pain, fatigue.
Cardiovascular: cardiac irregularities, hypertension, myocardial infarction, hypotension including orthostatic hypotension, palpitation, phlebitis, syncope.
Gastrointestinal: anorexia, bruxism, burning sensation of the tongue, constipation, dark saliva, development of duodenal ulcer, diarrhea, dry mouth, dyspepsia, dysphagia, flatulence, gastrointestinal bleeding, gastrointestinal pain, heartburn, hiccups, sialorrhea, taste alterations, vomiting.
Hematologic: hemolytic and non-hemolytic anemia, leukopenia, thrombocytopenia, agranulocytosis.
Hypersensitivity: angioedema, urticaria, pruritus, Henoch-Schonlein purpura, bullous lesions (including pemphigus-like reactions).
Metabolic: edema, weight gain, weight loss.
Musculoskeletal: back pain, leg pain, muscle cramps, shoulder pain.
Nervous System/Psychiatric: agitation, anxiety, ataxia, blepharospasm (which may be taken as an early sign of excess dosage; consideration of dosage reduction may be made at this time), bradykinetic episodes ("on-off" phenomenon), confusion, decreased mental acuity, disorientation, euphoria, dizziness, dream abnormalities including nightmares, extrapyramidal disorder, falling, gait abnormalities, headache, increased tremor, insomnia, memory impairment, muscle twitching, nervousness, numbness, paresthesia, peripheral neuropathy, somnolence, trismus, activation of latent Horner's syndrome, increased libido.
Respiratory: upper respiratory infection, dyspnea, pharyngeal pain, cough.
Skin: flushing, increased sweating, malignant melanoma (see also **CONTRAINDICATIONS**), rash, alopecia, dark sweat.
Special Senses: oculogyric crises, diplopia, blurred vision, dilated pupils.
Urogenital: dark urine, priapism, urinary frequency, urinary incontinence, urinary retention, urinary tract infection.
Laboratory Tests: abnormalities in alkaline phosphatase, SGOT (AST), SGPT (ALT), lactic dehydrogenase, bilirubin, blood urea nitrogen (BUN), Coombs test; elevated serum glucose; decreased hemoglobin and hematocrit; decreased white blood cell count and serum potassium; increased serum creatinine and uric acid; white blood cells, bacteria and blood in the urine; protein and glucose in the urine.
Miscellaneous: bizarre breathing patterns, faintness, hoarseness, hot flashes, malaise, neuroleptic malignant syndrome, sense of stimulation.

OVERDOSAGE

No reports of overdose with LODOSYN have been received. Management of overdosage with carbidopa is the same as that with levodopa or carbidopa-levodopa preparations.
In the event of overdosage, general supportive measures should be employed, along with immediate gastric lavage. Intravenous fluids should be administered judiciously, and an adequate airway maintained. Electrocardiographic monitoring should be instituted and the patient carefully observed for the development of arrhythmias; if required, appropriate antiarrhythmic therapy should be given. The possibility that the patient may have taken other drugs as well as LODOSYN should be taken into consideration. To date, no experience has been reported with dialysis; hence, its value in overdosage is not known. Pyridoxine is not effective in reversing the actions of LODOSYN.
Based on studies in which high doses of levodopa and/or carbidopa were administered, a significant proportion of rats and mice given single oral doses of levodopa of approximately 1500-2000 mg/kg are expected to die. A significant proportion of infant rats of both sexes are expected to die at a dose of 800 mg/kg. A significant proportion of rats are expected to die after treatment with similar doses of carbidopa. The addition of carbidopa in a 1:10 ratio with levodopa increases the dose at which a significant proportion of mice are expected to die to 3360 mg/kg.

DOSAGE AND ADMINISTRATION

Whether given with SINEMET (Carbidopa-Levodopa) or with levodopa, the optimal daily dosage of LODOSYN must be determined by careful titration. Most patients respond to a 1:10 proportion of carbidopa and levodopa, provided the daily dosage of carbidopa is 70 mg or more a day. The maximum daily dosage of carbidopa should not exceed 200 mg, since clinical experience with larger dosages is limited. If the patient is taking SINEMET (Carbidopa-Levodopa), the amount of carbidopa in SINEMET (Carbidopa-Levodopa) should be considered when calculating the total amount of LODOSYN to be administered each day.

Patients Receiving SINEMET (Carbidopa-Levodopa) Who Require Additional Carbidopa

Some patients taking SINEMET (Carbidopa-Levodopa) may not have adequate reduction in nausea and vomiting when the dosage of carbidopa is less than 70 mg a day, and the dosage of levodopa is less than 700 mg a day. When these patients are taking SINEMET 10-100** (Carbidopa-Levodopa), 25 mg of LODOSYN may be given with the first dose of SINEMET (Carbidopa-Levodopa) each day. Additional doses of 12.5 mg or 25 mg may be given during the day with each dose of SINEMET (Carbidopa-Levodopa). When patients are taking SINEMET 25-250*** (Carbidopa-Levodopa) or SINEMET 25-100† (Carbidopa-Levodopa), 25 mg of LODOSYN may be given with any dose of SINEMET (Carbidopa-Levodopa) as required for optimum therapeutic response. The maximum daily dosage of carbidopa, given as LODOSYN and as SINEMET (Carbidopa-Levodopa), should not exceed 200 mg.

**SINEMET 10-100 (Carbidopa-Levodopa) contains 10 mg of carbidopa and 100 mg of levodopa.

***SINEMET 25-250 (Carbidopa-Levodopa) contains 25 mg of carbidopa and 250 mg of levodopa.

†SINEMET 25-100 (Carbidopa-Levodopa) contains 25 mg of carbidopa and 100 mg of levodopa.

Patients Requiring Individual Titration of Carbidopa and Levodopa Dosage

Although SINEMET (Carbidopa-Levodopa) is the preferred method of carbidopa and levodopa administration, there may be an occasional patient who requires individually titrated doses of these two drugs. **In these patients, LODOSYN (Carbidopa) should be initiated at a dosage of 25 mg three or four times a day. The two drugs should be given at the same time, starting with no more than one-fifth (20%) to one-fourth (25%) of the previous or recommended daily dosage of levodopa when given without LODOSYN (Carbidopa). In patients already receiving levodopa therapy, at least twelve hours should elapse between the last dose of levodopa and initiation of therapy with LODOSYN (Carbidopa) and levodopa. A convenient way to initiate therapy in these patients is in the morning following a night when the patient has not taken levodopa for at least twelve hours.** Physicians who prescribe separate doses of LODOSYN and levodopa should be thoroughly familiar with the directions for use of each drug.

Dosage Adjustment

Dosage of LODOSYN may be adjusted by adding or omitting one-half or one tablet a day. Because both therapeutic and adverse responses occur more rapidly with combined therapy than when only levodopa is given, patients should be monitored closely during the dose adjustment period. Specifically, involuntary movements will occur more rapidly when LODOSYN and levodopa are given concomitantly than when levodopa is given without LODOSYN. The occurrence of involuntary movements may require dosage reduction. Blepharospasm may be a useful early sign of excess dosage in some patients.

Current evidence indicates other standard antiparkinsonian drugs may be continued while carbidopa and levodopa are being administered. However, the dosage of such other standard antiparkinsonian drugs may require adjustment.

Interruption of Therapy

Sporadic cases of a symptom complex resembling the Neuroleptic Malignant Syndrome (NMS) have been associated with dose reductions and withdrawal of SINEMET (Carbidopa-Levodopa) or SINEMET CR (Carbidopa-Levodopa) Sustained-Release. Patients should be observed carefully if abrupt reduction or discontinuation of SINEMET (Carbidopa-Levodopa) or SINEMET CR (Carbidopa-Levodopa) Sustained-Release is required, especially if the patient is receiving neuroleptics. (See WARNINGS.)

If general anesthesia is required, therapy may be continued as long as the patient is permitted to take fluids and medication by mouth. When therapy is interrupted temporarily, the patient should be observed for symptoms resembling NMS, and the usual daily dosage may be resumed as soon as the patient is able to take medication orally.

HOW SUPPLIED

Tablets LODOSYN, 25 mg, are orange, round, compressed tablets, that are scored and coded 511 on one side and LODOSYN on the other.

They are supplied as follows:

NDC 0056-0511-68 bottles of 100.

Storage

Store at 25°C (77°F), excursions permitted to 15–30°C (59–86°F).

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